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(54) **METHODS FOR TREATING RESPIRATORY DISEASE**

METHODEN ZUR BEHANDLUNG VON ATEMWEGSERKRANKUNGEN

PROCEDES DE TRAITEMENT DES MALADIES RESPIRATOIRES

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(73) Proprietor: **Milkhaus Laboratory, Inc.**
Delanson, NY 12053 (US)

(72) Inventor: **MCMICHAEL, John**
Delanson, NY 12053 (US)

(74) Representative: **Brown, John David et al**
FORRESTER & BOEHMERT
Pettenkoferstrasse 20-22
80336 München (DE)

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- **CURRENT BIOLOGY LTD.**, Volume 5, issued 1994, **LEDLEY**, "Nonviral Gene Therapy", pages 626-636.
- **HUMAN GENE THERAPY**, Volume 6, issued September 1995, **LEDLEY**, "Nonviral Gene Therapy: the Promise of Genes as Pharmaceutical Products", pages 1129-1144.

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Description**FIELD OF THE INVENTION**

[0001] The present invention relates to treatment of pulmonary disorders.

BACKGROUND OF THE INVENTION

[0002] The present invention provides treatment of pulmonary diseases. Such diseases, including cystic fibrosis, emphysema, chronic bronchitis, sinusitis, and the common cold, have in common bronchial or sinus congestion, production of large amounts of sputum, and the possibility of secondary bacterial infection requiring antibiotic therapy. The most serious of those diseases is cystic fibrosis, a genetic disorder of exocrine function characterized by abnormally viscous mucus secretions leading to chronic pulmonary obstruction, pancreatic insufficiency and elevated sweat sodium and chloride levels. Cystic fibrosis is often fatal. The viscosity of sputum produced by cystic fibrosis patients is thought to be due to its high content of DNA. Diseases such as bronchitis, emphysema, sinusitis, and the common cold are generally less severe than cystic fibrosis, but those diseases also may result in production of large amounts of sputum. As with cystic fibrosis, other pulmonary diseases frequently lead to secondary bacterial infections.

[0003] Treatment of pulmonary diseases generally requires antibiotic therapy which is frequently ineffective. Recently, however, cystic fibrosis has been treated using DNase. The rationale for such therapy is that degrading DNA in sputum reduces the viscosity of the sputum and results in an increased ability of the patient to evacuate sputum from the lungs and nasal passage. However, no known report advocates using DNA itself as a treatment for any pulmonary infection.

[0004] It is noted that WO 94/23048 discloses vectors for gene therapy of cystic fibrosis, WO93/12240 discloses compositions comprising nucleic acids for gene therapy of cystic fibrosis, US Patent No. 5240846 discloses a gene therapy of cystic fibrosis, Science, Volume 252, pages 431-434 (19 April 1991) discloses somatic gene therapy for, inter alia, cystic fibrosis and Current Biology Ltd, Volume 5, pages 626-636 (1994) discloses non-viral gene therapy for, inter alia cystic fibrosis.

SUMMARY OF THE INVENTION

[0005] The present provides the use of an effective amount of DNA in a pharmaceutically - acceptable vehicle for the manufacture of a medicament for relieving respiratory congestion in a patient, in a manner so as not to effect gene transfer, of the patient having a disease characterized by respiratory congestion. In a preferred embodiment, the invention provides for reducing congestion in a patient having a respiratory illness. The invention results in reduced viscosity of mucus, in-

creased productivity of respiratory congestion and reduced accumulation of mucus in the respiratory and nasal passages.

[0006] Methods comprise administration to a patient suffering from respiratory congestion an effective amount of DNA. The DNA is preferably provided in an amount ranging from 0.00012 mg to 0.003 mg and is preferably formulated in a liquid vehicle and provided at a concentration of approximately 0.0006 mg as single drops. A preferred route of administration is sublingual, but other routes, such as intravenous, intramuscular, and intrathecal are expected to work. DNA for use in the present invention may be prokaryotic DNA or eukaryotic DNA pharmaceutically-acceptable vehicles, including water, saline, albumin, and dextrose.

[0007] Additional aspects and advantages of the invention will become apparent upon consideration of the following detailed description thereof.

DETAILED DESCRIPTION OF THE INVENTION

[0008] The present invention provides for treating patients with pulmonary disease by administering to such patients a small amount of DNA.

[0009] The present invention is useful for treating pulmonary congestion in patients having any disease in which mucus production is a symptom and is especially effective in treating diseases wherein viscous mucus or sputum is produced and becomes lodged in a patient's respiratory tract. In those cases, the invention reduces production of DNA in a patient's mucus secretions and thereby render mucus less viscous, allowing for increased production away from the respiratory tract.

[0010] The invention has been tested in clinical trials with human patients having various respiratory disorders, including cystic fibrosis, bronchitis, and emphysema using calf thymus DNA (Sigma, St. Louis). In each case, patients are administered sublingual drops of DNA at a concentration of about 0.0006 mg DNA per drop. No other therapy was conducted in any patient during the course of DNA therapy. As noted below, all patients tested showed improvement in mucus production (i.e. sputum was easier to dislodge) from the respiratory tract. In addition, sputum was less viscous as compared to pretreatment levels. Reduced sputum viscosity leads to increased patient comfort, increased ability of the patient to breathe, and reduced risk of secondary bacterial infection. No adverse side effects were observed in any patients. Drops of DNA may be administered at the appropriate concentration in doses of 1 to 10 drops per day as required by the patient. For each Example below, calf thymus DNA (Sigma) was used.

[0011] The following Examples illustrate the preferred embodiments of the invention and provide evidence of the effectiveness of the treatment methods. Numerous improvements and further aspects of the invention are apparent to the skilled artisan upon consideration of the Examples which follow.